

REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections set forth in the Office action dated November 19, 2002 are respectfully requested.

The Invention.

The present invention is directed to DNA sequences, vectors and cells for enhanced secretion of glycosyltransferases, e.g., sialyltransferase, galactosyltransferase and fucosyltransferase, from filamentous fungi (particularly *Aspergillus*). Surprisingly, the invention may be used to secrete the normally membrane bound glycosyltransferases.

Status of the Application.

Claims 11-18 are pending in the application.

Claim 11 has been amended by the present response. Support for this amendment may be found throughout the specification. See, for example, page 12, second full paragraph. No new matter is introduced by these amendments.

Applicants have amended the specification to present the Sequence Listing in accord with 37 CFR §1.821 through 1.825. The specification has further been amended in accordance with 37 C.F.R. §1.821(d) to correctly identify sequences by sequence identifiers preceded by SEQ ID NO:.. No new matter is introduced by way of these amendments.

35 U.S.C. §112, second paragraph

Claims 11, 15 and 18 stand rejected under 35 USC §112, second paragraph as being indefinite. Specifically, the Examiner asserts that the phrase "secreted polypeptide or a portion thereof" renders the metes and bounds of the claim unclear. Applicants respectfully traverse the rejection.

Applicants on page 14 state "all or part of the mature sequence of the secreted polypeptide is used in the construction of the fusion DNA sequences." Applicants further state on page 16 "As used herein a "portion" of a secreted polypeptide is defined functionally as that portion of a secreted polypeptide which when combined with the other components of the fusion polypeptide defined herein results in increased secretion of the desired polypeptide as compared to the level of desired polypeptide secreted when an expression vector is used which does not utilize the secreted polypeptide. Generally, such portions of the secreted polypeptide comprise greater than 50% of the secreted polypeptide." Applicants provide guidance as to what portion of the secreted polypeptide is generally necessary and also provide methods by which to determine if there is increased secretion of the desired polypeptide. Thus, a skilled artisan would be able to

determine whether or not the portion of the secreted polypeptide used resulted in an increase in secretion of the desired polypeptide, i.e., a glycosyltransferase. Applicants respectfully request that the rejection be withdrawn.

Claim 11 and claims 12-18, which depend from claim 11, are rejected under 35 USC §112, second paragraph as being indefinite. Specifically, the recitation of the phrase "a fusion polypeptide comprising from the 5' end..." is deemed unclear as it is not conventional to refer to a 5' end of a polypeptide. Applicants have amended claim 11 to use conventional terminology. Withdrawal of the rejection is respectfully requested.

Claim 11 and claims 12-18, which depend from claim 11, are rejected under 35 USC §112, second paragraph as being indefinite. Specifically, the recitation of the phrase "amino acid sequence encoding a ..." uses an incorrect phrase, i.e., encoding. Applicants have amended claim 11 to recite "comprising" as suggested by the Examiner. Withdrawal of the rejection is respectfully requested.

Claim 11 and claims 12-18, which depend from claim 11, are rejected under 35 USC §112, second paragraph as being indefinite. Specifically, the phrase "normally secreted from *Aspergillus*" is deemed unclear. Applicants respectfully traverse the rejection.

"Normal" is defined as "Functioning or occurring in a natural way" in the Websters II New College Dictionary, appended hereto as Attachment A. Furthermore, Applicants on page 13 state "...preferred secreted polypeptides are those which are naturally secreted by the *Aspergillus* expression host." Thus, normal meaning of the work as well as the specification, taken as a whole, would lead one skilled in the art to use a polypeptide that is naturally secreted by *Aspergillus*. Applicants assert that the metes and bounds of the invention are clear. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §103(a).

Claims 1-10 stand rejected under 35 USC §103(a) as being unpatentable over either Lawlis (a) et al. (US Pat. No. 5,679,543) or Lawlis (b) et al. (US Pat. No. 6,130,063) and Kitagawa et al. (BBRC (1994) 194(1):375-382) or Ward et al (Biotechnology (1990) 8:435-440) and Kitagawa et al. Applicants respectfully traverse the rejections.

Lawlis (a or b) teach that heterologous proteins may be secreted at enhanced levels as fusion proteins compared to the levels achieved when it is not fused to a secreted *Aspergillus* polypeptide. However, Lawlis fails to describe a fusion polypeptide that is encompassed by the presently amended claims. It fails to teach or suggest that a normally membrane-bound enzyme such as a glycosyltransferase can be secreted.

Similarly, Ward et al. is concerned with the improvement in the secretion of a normally secreted enzyme, chymosin. There is nothing in Ward that teaches or suggests that a normally membrane-bound enzyme can be secreted if produced as a fusion polypeptide.

Kitagawa et al. fails to correct any deficiencies in either Lawlis (b) or Ward. Kitagawa is directed to the expression of a sialyltransferase in mammalian cells. Furthermore, Kitagawa fails to teach a secretion signal functional in *Aspergillus*.

Thus, the cited references, alone or in combination, fail to teach the presently claimed invention. Withdrawal of the rejection is respectfully requested.

Double Patenting

Claims 11-18 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-26 of US Patent No. 5,679,543 or claims 17-26 of US Patent No. 6,130,063 in view of Kitagawa et al.

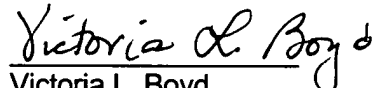
The patents fail to claim, alone or in combination, the present invention. The cited reference fails to correct any deficiencies nor does it provide a basis for the instant rejection. The reasons given above for the 35 USC §103 rejections are applicable to the double patenting rejection. Withdrawal of the rejection is respectfully requested.

Conclusion

In light of the above amendments, as well as the remarks, the Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7615.

Respectfully submitted,

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